Amendments to the Claims:

Please amend the Claims as follows.

1. (Previously Presented) An isolated monoclonal antibody that binds specifically to a polypeptide comprising a ubiquitination-regulating domain, or a functional fragment thereof, of a human TSG1O1 protein comprising the amino acid sequence of SEQ ID NO: 1, wherein said antibody binds specifically to said ubiquitination-regulating domain, or functional fragment thereof; and

wherein said antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ NO: 1.

2-3. (Canceled)

4. (Currently Amended) The antibody of Claim 1, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of SEQ ID NO:1, and wherein said epitope is found in amino acid residues 50-140 of SEQ ID NO:1.

5. (Previously Presented) The antibody of Claim 1, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of SEQ ID NO: 1, and wherein said epitope is found in amino acid residues 1-140 of SEQ ID NO:1.

6. (Previously Presented) The antibody of Claim 1, wherein said ubiquitination-

regulating domain comprises amino acid residues 140-250 of SEQ ID NO: 1, and wherein said epitope is found in amino acid residues 140-250 of SEQ ID NO:1.

7. (Withdrawn) A method of producing an antibody that binds specifically to an ubiquitination-regulating domain, comprising raising said antibody against a polypeptide comprising said ubiquitination-regulating domain.

8. (Withdrawn) The method of Claim 7, wherein said ubiquitination-regulating domain is a ubiquitination-regulating domain, or a functional fragment thereof, of a TSG1O1 protein.

9. (Withdrawn) The method of Claim 8, wherein said TSG 101 protein is a human TSG1O1 protein.

10. (Withdrawn) The method of Claim 9, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of said human TSGI 01 protein.

11. (Withdrawn) The method of Claim 8, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of said human TSG 101 protein.

12. (Withdrawn) The method of Claim 9, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of said human TSG1OI protein.

13. (Withdrawn) A method of treating a condition in a subject, said condition resulting from a change in a level of MDM2 protein in cells of said subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent comprising an ubiquitination-regulating domain.

14. (Withdrawn) A method of treating a condition in a subject, said condition resulting from a change in a level of a TSG 101 protein in cells of said subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent modulating the interaction of said TSG1OI protein with MDM2.

15. (Withdrawn-Previously Amended) A method for treatment of a proliferative disease in a subject comprising:

(a) monitoring the subject for a level of p53; and

(b) treating the subject with an agent so as to maintain said level of p53 within a target range, wherein said agent comprises an ubiquitination-regulating domain.

16. (Withdrawn-Previously Presented) A method for treatment of a proliferative disease in a subject comprising:

(a) monitoring the subject for a level of TSGI 01; and

(b) treating a subject with an agent so as to maintain said level of TSGIO1 within a target range, wherein said agent modulates the interaction of said TSG1O1 with MDM2.

17-21. (Canceled).

22. (Withdrawn) A method for treating a proliferative disease in a subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent modulating the interaction of a TSG1O1 protein with MDM2.

23. (Withdrawn) A cell comprising a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence such that said cell expresses said ubiquitination-regulating domain.

24. (Withdrawn) A cell comprising (i) a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence; and (ii) a polynucleotide encoding MDM2 protein operationally linked to a regulatory sequence, such that said cell expresses said ubiquitination-regulating domain and said MDM2 protein.

25. (Withdrawn) A cell comprising (i) a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence; (ii) a polynucleotide encoding MDM2 protein operationally linked to a regulatory sequence; and (iii) a polynueleotide encoding p53 protein operationally linked to a regulatory sequence, such that said cell expresses said ubiquitination-regulating domain, said MDM2 protein, and said p53 protein.

26-30. (Canceled).

31. (Withdrawn) A method of identifying an agent that modulates the interaction of a

TSGIOI protein with MDM2, comprising screening candidate agents using a screening assay comprising a cell expressing MDM2 and a polypeptide comprising an ubiquitination-regulating domain, or a functional fragment thereof, of said TSG1O1 protein.

32. (Withdrawn-Previously Amended) A method of identifying an agent that is capable of modulating the interaction of a TSGIO1 protein with MDM2, comprising:

(a) contacting a first cell expressing MDM2 and a polypeptide comprising an ubiquitination-regulating domain, or a functional fragment thereof, of said TSG 101 protein with said agent and measuring MDM2 level in said first cell;

(b) contacting a second cell expressing MDM2 but not an ubiquitination-regulating domain, or a functional fragment thereof, of said TSGIO1 protein, with said agent and measuring MDM2 level in said second cell; and

(c) comparing MDM2 levels measured in (a) and (b),

wherein a difference in MDM2 levels compared in step (c) identified said agent as capable of modulating the interaction of the TSG 101 protein with MDM2.

33-36. (Canceled).

37. (Withdrawn) A method of modulating a level of MDM2 in a cell, comprising contacting said cell with a polypeptide or derivative thereof that comprises a polypeptide comprising a polypeptide comprising an ubiquitination-regulating domain.

38. (Withdrawn) A method of modulating a level of p53 in a cell, comprising contacting said cell with a polypeptide or derivative thereof that comprises a polypeptide

comprising an ubiquitination-regulating domain.

39. (Withdrawn) A method of modulating a level of TSG1O1 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG 101 protein with MDM2.

40. (Withdrawn) A method of modulating a level of MDM2 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG 101 protein with MDM2.

41. (Withdrawn) A method of modulating a level of p53 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG1OI protein with MDM2.

42. (Withdrawn) A method for screening for a cellular protein that interacts with an ubiquitination-regulating domain, comprising identifying a cellular protein that binds said ubiquitination-regulating domain.

43. (Previously Presented) A pharmaceutical composition for treatment of diseases involving TSG 101-mediated ubiquitination, comprising:

an isolated monoclonal antibody that binds specifically to a polypeptide comprising an ubiquitination-regulating domain, or a functional fragment thereof, of a human TSG101 protein comprising the amino acid sequence of SEQ ID NO:1, wherein said antibody binds specifically

to said ubiquintination-regulating domain, or functional fragment thereof,

wherein said antibody binds specifically to an epitope in the ubiquitination regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ ID NO: 1, and

a pharmaceutically acceptable excipient.

44. (Withdrawn) A method for treatment of diseases involving TSG1OI-mediated ubiquitination, said method comprising:

administering to a subject suffering from a disease involving TSG1O1-mediated ubiquitination an effective amount of the pharmaceutical composition of Claim 43.

45. (Withdrawn) The method of Claim 44, wherein the diseases involving TSG 101-mediated ubiquitination comprise proliferative diseases, neurodegenerative diseases, autoimmune diseases, and developmental abnormalities.

46. (Previously Presented) An isolated monoclonal antibody that binds specifically to a ubiquitination-regulating domain of TSG101, or a functional fragment thereof, wherein said domain consists of amino acid residues 1-250 of SEQ ID NO: 1, and

wherein said antibody specifically binds to an epitope in the ubiquitination regulating domain of TSG101 protein found in amino acid residues 1-250 of SEQ ID NO: 1.

47. (Currently Amended) The isolated antibody of Claim 46, wherein said ubiquitination-regulating domain consists <u>of</u> amino acid residues 50-140 of SEQ ID NO: 1, or a

functional fragment thereof, and wherein said epitope is found in amino acid residues 50-140 of SEQ ID NO:1.

48. (Currently Amended) The isolated antibody of Claim 46, wherein said ubiquitination-regulating domain consists of amino acid residues 1-140 of SEQ ID NO: 1, or a functional fragment thereof, and wherein said epitope is found in amino acid residues 1-140 of SEQ ID NO:1.

49. (Currently Amended) The isolated antibody of Claim 46, wherein said ubiquitination regulating domain consists of amino acid residues 140-250 of SEQ ID NO: 1, or a functional fragment thereof, and wherein said epitope is found in amino acid residues 140-250 of SEQ ID NO:1.

50. (Currently Amended) A pharmaceutical composition for treatment of diseases involving TSG 101-mediated ubiquitination, comprising:

an isolated monoclonal antibody that binds specifically to a ubiquitination-regulating domain of human TSG101, or a functional fragment thereof, wherein said antibody binds specifically to an epitope in the ubiquitination-regulating domain of TSG101 protein found in amino acids 1-250 of SEQ ID NO: 1; and, a pharmaceutically acceptable excipient.